(FILE 'HOME' ENTERED AT 17:16:48 ON 13 NOV 2003)

FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CANCERLIT, CAPLUS, CEN, DISSABS, DGENE, DRUGB, DRUGLAUNCH, DRUGMONOG2, DRUGNL, DRUGU, EMBAL, EMBASE, ESBIOBASE, IFIPAT, IPA, JICST-EPLUS, KOSMET, LIFESCI, MEDICONF, MEDLINE, NAPRALERT, NLDB, NUTRACEUT, ..' ENTERED AT 17:17:03 ON 13 NOV 2003

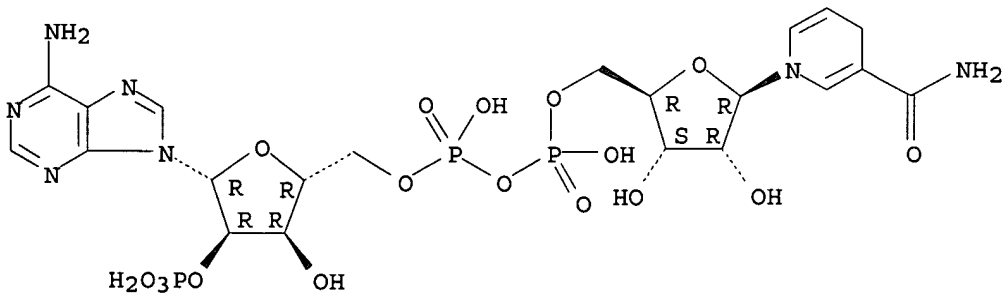
L1 1062 S CARDIOVASCULAR/AB AND SIMVASTATIN/AB
L2 302 DUP REM L1 (760 DUPLICATES REMOVED)
L3 69 S L2 AND PD<1999
L4 21 S L3 AND (SIMVASTATIN OR CARDIVASCULAR)/TI
L5 295 S HYPERTENSION/AB AND SIMVASTATIN/AB
L6 0 S L5 AND (NONHYPERCHOLESTEROLEMIC OR NONHYPERLIPIDEMIC OR NON

FILE 'USPATFULL' ENTERED AT 17:27:17 ON 13 NOV 2003
L7 1519 S SIMVASTATIN
L8 703 S L7 AND (FIBRILLATION OR ANGINA OR ANGINA OR TACHYCARDIA OR
L9 9 S L8 AND (NON-HYPERLIPIDEMIC OR NON-HYPERCHOLESTEROLEMIC OR N

=>

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN 53-57-6 REGISTRY
CN Adenosine 5'-(trihydrogen diphosphate), 2'-(dihydrogen phosphate), P'.fwdarw.5'-ester with 1,4-dihydro-1-.beta.-D-ribofuranosyl-3-pyridinecarboxamide (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Adenosine, 2'-(dihydrogen phosphate) 5'-(trihydrogen pyrophosphate), 5'.fwdarw.5'-ester with 1,4-dihydro-1-.beta.-D-ribofuranosylnicotinamide (8CI)
OTHER NAMES:
CN .beta.-NADPH
CN .beta.-Nicotinamide-adenine-dinucleotide-phosphoric acid
CN .beta.-TPNH
CN Codehydrase II, reduced
CN Codehydrogenase II, reduced
CN Coenzyme II, reduced
CN Cozymase II, reduced
CN Dihydrocodehydrogenase II
CN **NADPH**
CN NADPH2
CN Nicotinamide-adenine dinucleotide phosphate, reduced
CN Reduced codehydrogenase II
CN Reduced nicotinamide adenine dinucleotide phosphate
CN Reduced triphosphopyridine nucleotide
CN TPNH
CN Triphosphopyridine nucleotide, reduced
FS STEREOSEARCH
DR 22046-90-8, 3545-01-5
MF C21 H30 N7 O17 P3
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, MRCK*, NIOSHTIC, PROMT, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: EINECS**, NDSL**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.

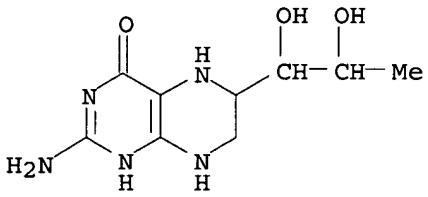


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9999 REFERENCES IN FILE CA (1907 TO DATE)
197 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
10018 REFERENCES IN FILE CAPLUS (1907 TO DATE)
57 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> d l2

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN 17528-72-2 REGISTRY
CN 4(1H)-Pteridinone, 2-amino-6-(1,2-dihydroxypropyl)-5,6,7,8-tetrahydro-
(9CI) (CA INDEX NAME)
OTHER NAMES:
CN 5,6,7,8-Tetrahydrobiopterin
CN **Tetrahydrobiopterin**
FS 3D CONCORD
DR 14443-70-0, 14901-24-7
MF C9 H15 N5 O3
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IPA, MEDLINE, PROMT, RTECS*, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)

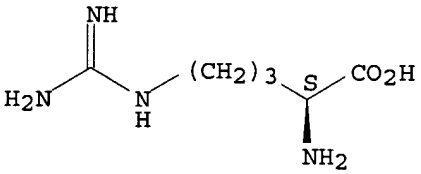


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1228 REFERENCES IN FILE CA (1907 TO DATE)
25 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1230 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2003 ACS on STN
RN 74-79-3 REGISTRY
CN **L-Arginine (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Arginine, L- (8CI)
OTHER NAMES:
CN (S)-2-Amino-5-[(aminoiminomethyl)amino]pentanoic acid
CN Arginine
CN L-(+)-Arginine
CN L-.alpha.-Amino-.delta.-guanidinovaleric acid
CN L-Arg
CN L-Norvaline, 5-[(aminoiminomethyl)amino]-
CN L-Ornithine, N5-(aminoiminomethyl)-
CN NSC 206269
CN Pentanoic acid, 2-amino-5-[(aminoiminomethyl)amino]-, (S)-
FS STEREOSEARCH
DR 7004-12-8, 142-49-4
MF C6 H14 N4 O2
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHAR, PHARMASEARCH, PIRA, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TULSA, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

37391 REFERENCES IN FILE CA (1907 TO DATE)
1023 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
37453 REFERENCES IN FILE CAPLUS (1907 TO DATE)
6 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

95-6428 001; NITRIC-OXIDE SYNTHASE ACTIVITY; CORONARY ENDOTHELIAL FUNCTION; RECOVERY OF NEONATAL LAMB HEARTS; L-ARGININE ENHANCES INJURY; COLD ISCHEMIA
95-8023 001; NITRIC-OXIDE SYNTHASE; RAT AORTA; MODULATION OF PULMONARY VASCULAR TONE

RE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)
BECKMAN J S	1990	87	1620	P NATL ACAD SCI USA
COHEN R A	1995	92	3337	CIRCULATION
COSENTINO F	1995	91	139	CIRCULATION
GIOVANELLI J	1991	88	7091	P NATL ACAD SCI USA
GROSS S S	1992	267	25722	J BIOL CHEM
HEINZEL B	1992	281	627	BIOCHEM J
HEVEL J M	1992	31	7160	BIOCHEMISTRY-US
HIGMAN D J	1996	16	546	ARTERIOSCL THROM VAS
KATUSIC Z S	1989	257	H1235	AM J PHYSIOL
KATUSIC Z S	1993	264	H859	AM J PHYSIOL
KATUSIC Z S	1995	92	391	CIRCULATION
KATUSIC Z S	1996	20	443	FREE RADICAL BIO MED
KAUFMAN S	1993	13	261	ANNU REV NUTR
KINOSHITA H	1996	271	H738	AM J PHYSIOL
KLATT P	1993	268	14781	J BIOL CHEM
KONTOS H A	1996	271	H1498	AM J PHYSIOL
LOWRY O H	1951	193	265	J BIOL CHEM
MAYER B	1990	277	215	FEBS LETT
MAYER B	1991	288	187	FEBS LETT
MAYER B	1995	351	453	N-S ARCH PHARMACOL
MCCORD J M	1969	244	6049	J BIOL CHEM
MOORE P K	1990	99	408	BRIT J PHARMACOL
NICHOL C A	1985	54	729	ANNU REV BIOCHEM
POU S	1992	267	24173	J BIOL CHEM
PRITCHARD K A	1995	77	510	CIRC RES
ROSENKRANZWEISS P	1994	93	2236	J CLIN INVEST
RUBANYI G M	1986	250	H822	AM J PHYSIOL
SAKAI N	1993	43	6	MOL PHARMACOL
SCHMIDT K	1992	281	297	BIOCHEM J
TIEFENBACHER C P	1996	94	1423	CIRCULATION
TSUTSUI M	1996	79	336	CIRC RES
WERNERFELMAYER G	1993	268	1842	J BIOL CHEM

=>

L24 ANSWER 19 OF 68 CAPLUS COPYRIGHT 2003 ACS on STN
TI **Nitric oxide** synthase in cat brain: cofactors - enzyme-substrate interaction
SO Free Radical Biology & Medicine (**1996**), 21(1), 109-115
CODEN: FRBMEH; ISSN: 0891-5849
AB NO, derived from **L-arginine** by **nitric oxide** synthase (NOS), is an activator of sol. guanylate cyclase and a cellular messenger. Here, the authors demonstrate that, in cat brain, the neuronal constitutive NOS activity is (1) **NADPH** /Ca2+-dependent, (2) independent of exogenous calmodulin in crude brain supernatant, (3) significantly enhanced by exogenous FAD and **tetrahydrobiopterin** (Vmax: 118 instead of 59.4 pmol of citrulline formed/mg protein/min), (4) inhibited by Ca2+ chelators and calmodulin antagonists, and (5) present in several neuroanatomical structures. Moreover, the Km for **L-arginine** was 11 .mu.M instead of 41 .mu.M in the presence of FAD and **tetrahydrobiopterin** in the incubation mixt., thus demonstrating that these cofactors are able to stabilize the enzyme-substrate interactions.
ST **nitric oxide** synthase brain cat
IT Kinetics, enzymic
Michaelis constant
(of **nitric oxide** synthase of cat brain)
IT Brain
(regional distribution of **nitric oxide** synthase in cat brain and characterization of enzyme cofactors and enzyme-substrate interactions)
IT 125978-95-2, **Nitric oxide** synthase
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(regional distribution of **nitric oxide** synthase in cat brain and characterization of enzyme cofactors and enzyme-substrate interactions)
IT **53-57-6**, **NADPH** 146-14-5, FAD 7440-70-2, Calcium, biological studies **17528-72-2**, **Tetrahydrobiopterin**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

L24 ANSWER 4 OF 68 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
TI **Nitric oxide** synthase in cat brain:
Cofactors-enzyme-substrate interaction.
SO Free Radical Biology and Medicine, (**1996**) Vol. 21, No. 1, pp.
109-115.
CODEN: FRBMEH. ISSN: 0891-5849.
AB **Nitric oxide**, derived from **L-arginine** by the enzyme **nitric oxide** synthase, is an activator of the soluble guanylate cyclase and a cellular messenger. This work demonstrates that, in cat brain, the neuronal constitutive **nitric oxide** synthase activity is a) **NADPH** /calcium dependent, b) independent upon exogenous calmodulin in crude brain supernatant, c) significantly enhanced by exogenous FAD and **tetrahydrobiopterin** (V-max: 118 instead of 59.4 pmol of citrulline formed cntdot mg of prot cntdot -1 min-1, d) inhibited by calcium chelators and calmodulin antagonist, and e) present in several neuroanatomical structures. Moreover, the K-m value for **L-arginine** was of 11 mu-M instead of 41 mu-M in the presence of FAD and **tetrahydrobiopterin** in the incubation mixture, thus demonstrating that these cofactors are able to stabilize the enzyme-substrate interactions.
IT Major Concepts
Biochemistry and Molecular Biophysics; Enzymology (Biochemistry and Molecular Biophysics); Nervous System (Neural Coordination)
IT Chemicals & Biochemicals
NITRIC OXIDE SYNTHASE; FAD; **TETRAHYDROBIOPTERIN**; **L-ARGININE**; **NADPH**
IT Miscellaneous Descriptors
BIOCHEMISTRY AND MOLECULAR BIOPHYSICS; BRAIN; CALMODULIN; COFACTORS-ENZYME-SUBSTRATE INTERACTION; EC 1.14.13; FAD; FREE RADICALS; **L-ARGININE**; **NADPH**; NEURAL COORDINATION/NERVOUS SYSTEM; **NITRIC OXIDE** SYNTHASE; **TETRAHYDROBIOPTERIN**
RN 125978-95-2 (**NITRIC OXIDE** SYNTHASE)
146-14-5 (FAD)
17528-72-2 (**TETRAHYDROBIOPTERIN**)
74-79-3 (**L-ARGININE**)
53-57-6 (**NADPH**)

L9 ANSWER 44 OF 46 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN

SO AMERICAN JOURNAL OF PHYSIOLOGY-HEART AND CIRCULATORY PHYSIOLOGY, (**AUG 1997**) Vol. 42, No. 2, pp. H718-H724.
Publisher: AMER PHYSIOLOGICAL SOC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
ISSN: 0363-6135.

AB **Tetrahydrobiopterin** is an essential cofactor in biosynthesis of nitric oxide. The present study was designed to determine the effect of decreased intracellular **tetrahydrobiopterin** levels on endothelial function of isolated cerebral arteries. Blood vessels were incubated for 6 h in minimum essential medium (MEM). . . . in the presence of a cyclooxygenase inhibitor, indomethacin (10(-5) M). In arteries with endothelium, DAHP significantly reduced intracellular levels of **tetrahydrobiopterin**. DAHP in combination with a **precursor** of the salvage pathway of **tetrahydrobiopterin** biosynthesis, sepiapterin (10(-4) NI), not only restored but increased levels of **tetrahydrobiopterin** above control values. In DAHP-treated arteries, endothelium-dependent relaxations to bradykinin (10(-10)-10(-6) M) Or calcium ionophore A23187 (10(-9)-10(-6) M) were significantly. . . bradykinin or A23187 in control arteries and in DAHP-treated arteries. These studies demonstrate that in cerebral arteries,decreased intracellular levels of **tetrahydrobiopterin** can reduce endothelium-dependent relaxations. Production of superoxide anions during activation of dysfunctional endothelial nitric oxide synthase appears to be responsible. . .

L9 ANSWER 44 OF 46 SCISEARCH COPYRIGHT 2003 THOMSON ISI on STN
AN 97:611092 SCISEARCH
GA The Genuine Article (R) Number: XQ295
TI Inhibition of tetrahydrobiopterin biosynthesis impairs endothelium-dependent relaxations in canine basilar artery
AU Kinoshita H; Milstien S; Wambi C; Katusic Z S (Reprint)
CS MAYO CLIN & MAYO FDN, DEPT ANESTHESIOL, 200 1ST ST SW, ROCHESTER, MN 55905 (Reprint); MAYO CLIN & MAYO FDN, DEPT ANESTHESIOL, ROCHESTER, MN 55905; MAYO CLIN & MAYO FDN, DEPT PHARMACOL, ROCHESTER, MN 55905; NIMH, LAB CELLULAR & MOL REGULAT, NIH, BETHESDA, MD 20892
CYA USA
SO AMERICAN JOURNAL OF PHYSIOLOGY-HEART AND CIRCULATORY PHYSIOLOGY, (**AUG 1997**) Vol. 42, No. 2, pp. H718-H724.
Publisher: AMER PHYSIOLOGICAL SOC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
ISSN: 0363-6135.
DT Article; Journal
FS LIFE
LA English
REC Reference Count: 32
AB **Tetrahydrobiopterin** is an essential cofactor in biosynthesis of nitric oxide. The present study was designed to determine the effect of decreased intracellular **tetrahydrobiopterin** levels on endothelial function of isolated cerebral arteries. Blood vessels were incubated for 6 h in minimum essential medium (MEM) in the presence or absence of a GTP cyclohydrolase I inhibitor, 2,4-diamino-6-hydroxypyrimidine (DAHP, 10(-2) M). Rings with and without endothelium were suspended for isometric force recording in the presence of a cyclooxygenase inhibitor, indomethacin (10(-5) M). In arteries with endothelium, DAHP significantly reduced intracellular levels of **tetrahydrobiopterin**. DAHP in combination with a **precursor** of the salvage pathway of **tetrahydrobiopterin** biosynthesis, sepiapterin (10(-4) NI), not only restored but increased levels of **tetrahydrobiopterin** above control values. In DAHP-treated arteries, endothelium-dependent relaxations to bradykinin (10(-10)-10(-6) M) Or calcium ionophore A23187 (10(-9)-10(-6) M) were significantly reduced, whereas endothelium-independent relaxations to a nitric oxide donor, 3-morpholinosydnonimine (10(-9)-10(-4) M), were not affected. When DAHP-treated arteries with endothelium were incubated with sepiapterin (10(-4) M) or superoxide dismutase (150 U/ml), relaxations to bradykinin and A23187 were restored to control levels. In contrast, superoxide dismutase did not affect endothelium-dependent relaxations in arteries incubated in MEM. A nitric oxide synthase inhibitor, N-G-nitro-L-arginine methyl ester (10(-4) M), abolished relaxations to bradykinin or A23187 in control arteries and in DAHP-treated arteries. These studies demonstrate that in cerebral arteries,decreased intracellular levels of **tetrahydrobiopterin** can reduce endothelium-dependent relaxations. Production of superoxide anions during activation of dysfunctional endothelial nitric oxide synthase appears to be responsible for the impairment of endothelial function.
CC PHYSIOLOGY
ST Author Keywords: cerebral artery; nitric oxide; receptors; superoxide anions; sepiapterin
STP KeyWords Plus (R): NITRIC-OXIDE SYNTHASE; RELAXING FACTOR; SMOOTH-MUSCLE; CYCLIC-GMP; SUPEROXIDE; GENERATION; COFACTOR; CELLS; REQUIREMENT; ARGININE
RF 95-0388 002; NITRIC-OXIDE SYNTHASE; ALDEHYDE FIXATION DIFFERENTIALLY AFFECTS DISTRIBUTION OF DIAPHORASE ACTIVITY; LIGHT-INDUCED FOS EXPRESSION
95-2155 001; SUPEROXIDE-DISMUTASE ACTIVITY; OXIDATIVE STRESS; @4FE-4S* CLUSTER-CONTAINING ENZYME IN ESCHERICHIA-COLI
95-2212 001; PEROXYNITRITE IN-VITRO; NITRIC-OXIDE SYNTHASE; HYDROXYL RADICAL; FORMATION OF 8-NITROGUANINE; PC12 CELLS
95-6407 001; INDUCIBLE NITRIC-OXIDE SYNTHASE; ENHANCED ANTITHROMBOTIC ACTIVITY; RAT CARDIAC MYOCYTES